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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/672,142	09/26/2003	David J. Yang	UTSC:664USC2	6122

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EXAMINER	
JONES, DAMERON	
ART UNIT	**PAPER NUMBER**
1616	

DATE MAILED: 03/08/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/672,142	YANG ET AL.	
	Examiner	Art Unit	
	D. L. Jones	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *9/26/03; 4/12/04; 6/1/04; and 12/20/04*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *52-83* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *52-83* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *4/12/04 & 6/1/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

ACKNOWLEDGMENTS

1. The Examiner acknowledges receipt of the amendment filed 9/26/03 wherein the specification was amended; claims 1-51 were canceled; and claims 52-83 were added. In addition, the Examiner acknowledges receipt of the amendment filed 12/20/04 wherein the specification was amended.

Note: Claims 52-83 are pending.

APPLICANT'S INVENTION

2. Applicant's invention is directed to a method of delivering a radionuclide to a target as set forth in independent claim 52.

DOUBLE PATENTING REJECTIONS

3. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double

patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

4. Claims 52-62, 64, and 67-83 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 32, and 38-41 of copending Application No. 10/732,919. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are directed to a method of obtaining a radioactive signal (i.e., image) from the administered targeting ligand. The claims differ in 10/732,919 reads on specific targets whereas the instant invention is not limited to any particular target.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

5. Claims 52-59, 64, and 67-79 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 38-41 and 60 of copending Application No. 09/599,152. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are directed to obtaining a radioactive signal (i.e., image) from the

administered targeting ligand. The claims differ in that claim 38 of 09/599,152 *generally* discloses all the components set forth in the instant invention. Thus, a skilled practitioner in the art would recognize that claim 38 of the pending application is more specific in the tissue specific ligands being claimed. Furthermore, 09/599,152 specifically discloses that the method is for imaging whereas in the instant invention, it is disclosed that a radioactive signal is generated from the administer ligand conjugate. However, a skilled practitioner in the art would recognize that imaging results form administering the labeled compound which give off a signal.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

6. Claims 52, 56-59, and 64-66 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 38-41 of copending Application No. 10/672,763. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are directed to the use of a radiolabeled EC composition that is administered to a subject. The claims differ in that claim 38 of 10/672,763 specifically discloses that the method is for imaging whereas in the instant invention, it is disclosed that a radioactive signal is generated from the administer ligand conjugate. However, a skilled practitioner in the art would recognize that imaging results form administering the labeled compound which give off a signal.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

7. Claims 52, 56, 57 and 64-66 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 2, 27, 28, and 34-37 of copending Application No. 10/703,405. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are directed to obtaining a radioactive signal (i.e., image) from the administered targeting ligand. The claims differ in that claim 34 of 10/703,405 specifically discloses that the method is for imaging whereas in the instant invention, it is disclosed that a radioactive signal is generated from the administer ligand conjugate. However, a skilled practitioner in the art would recognize that imaging results form administering the labeled compound which give off a signal.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

102 REJECTIONS

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claims 52, 53, 55, 64, and 65 are rejected under 35 U.S.C. 102(b) as being anticipated by Anderson et al (Nucl. Med. Biol., 1995, 22(2), pages 165-173).

Anderson et al disclose ethylenedicysteine (EC) complexes of Ga (III) and In(III) in in vivo studies. EC is a N22S2 ligand that contains tow carboxylic acid moieties for complexation to gallium and indium. Thus, 67Ga- and 111In-labeled complexes of EC were prepared and evaluated in mammals (see entire document, especially, abstract; page 167, 'Animal studies'; page 171, 'In vivo studies'; page 171, Table 5). The radioactive complexes were analyzed in the lung, liver, and brain (page 168, left column, first paragraph). Thus, both Applicant and Anderson et al disclose a method of delivering a radionuclide labeled bisaminoethanethiol targeting ligand conjugate to a subject.

103 REJECTIONS

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. Claims 52, 53, 55-57, 60-62, 64-69, and 72 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yang et al (J. Labelled Compd. Radiopharm., 42, Suppl. 1, 1999, pp. S696-S697).

Yang et al disclose the imaging of tumor folate receptors using radiolabeled folate and methotrexate. The study was specifically directed to 99mTc-labeled folic acid using ethylenedicysteine (EC) as a chelator and In-111 labeled DTPA-methotrexate which were used to image tumor folate receptors in vivo. 99m-TC-EC-folate was analyzed in breast tumor bearing rats. The 99m-Tc-EC-folate was co-administered with folic acid to tumor bearing rats (see entire document, especially, page S696).

Thus, it would have been obvious to one of ordinary skill in the art at the time the invention was made to deliver a radionuclide complex to a subject since both the cited prior art and the instant invention are directed to a method of delivering a radionuclide to target cells in vivo wherein a composition comprising a radiolabeled bis-aminoethanethiol targeting ligand conjugate is utilized.

12. Claims 52-57, 60-69, 72, and 73 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ilgan et al (Cancer Biotherapy & Radiopharmaceuticals, 13(6), 1998, pages 427-435).

Ilgan et al disclose 99mTc-ethylenedicysteine folate as a tumor imaging agent and the evaluation of the complex in vivo. In particular, cellular accumulation of folate and folate analogs such as methotrexate are found on various tumor cells (see entire document, especially, abstract). In addition, Ilgan et al disclose that folate receptors are overexpressed on may neoplastic cell types such as lung, breast, ovarian, cervical, colorectal, nasopharyngeal, renal adenocarcinomans, malign melanoma, and

ependymomas (page 428, left column, first paragraph). On page 431, Tables 2 and 3, the 99mTc-EC-folate in breast tumor bearing rats is disclosed.

Thus, it would have been obvious to one of ordinary skill in the art at the time the invention was made to deliver a radionuclide complex to a subject since both the cited prior art and the instant invention are directed to a method of delivering a radionuclide to target cells in vivo wherein a composition comprising a radiolabeled bis-aminoethanethiol targeting ligand conjugate is utilized.

13. Claims 52, 53, 55-57, 60-62, 64-66, 74, and 75 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yang et al (Pharmaceutical Research, 16(5), 1999, pages 743-750).

Yang et al disclose the non-invasive assessment of tumor hypoxia with 99m-Tc-labeled metronidazole. 99m-Tc-labeled metronidazole (MN) was labeled using ethylenedicysteine (EC) as a chelator. The 99mTc-EC-MN was determined in breast tumor bearing subjects (see entire document, especially, abstract). Tables 1 and 2, pages 745-746, discloses the biodistribution of 99m-Tc-EC-MN.

Thus, it would have been obvious to one of ordinary skill in the art at the time the invention was made to deliver a radionuclide complex to a subject since both the cited prior art and the instant invention are directed to a method of delivering a radionuclide to target cells in vivo wherein a composition comprising a radiolabeled bis-aminoethanethiol targeting ligand conjugate is utilized.

14. Claims 52, 53, 55-57, 60-62, 64-67, 74, and 75 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zareneyrizi et al Anti-Cancer Drugs, 1999, 10, pp. 685-692).

Zareneyrizi et al disclose the synthesis of 99m-Tc-ethylenedicysteine (EC) colchicine in the evaluating of tumor microvascular density. 99mTc-EC colchicines was evaluated in breast tumor bearing subjects (see entire document, especially, abstract; pages 687-688, 'Tissue distribution studies').

Thus, it would have been obvious to one of ordinary skill in the art at the time the invention was made to deliver a radionuclide complex to a subject since both the cited prior art and the instant invention are directed to a method of delivering a radionuclide to target cells in vivo wherein a composition comprising a radiolabeled bis-aminoethanethiol targeting ligand conjugate is utilized.

COMMENTS/NOTES

15. Applicant is reminded that the recitation that an element is 'capable of' performing a function is not a positive limitation, but only requires the ability to so perform that function (see claim 52, lines 3-4).

16. The lined through document (C204) on the information disclosure statement was not present in the file during examination. Thus, Applicant is respectfully requested to submit the document for consideration along with the next correspondence to the Examiner.

17. Applicant is respectfully requested to submit the year of the Vega et al document (C258) listed on the information disclosure statement. The document was lined through because the year of publication was not present; however, the document was considered.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to D. L. Jones whose telephone number is (571) 272-0617. The examiner can normally be reached on Mon.-Fri., 6:45 a.m. - 3:15 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on (571) 272-0887. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

D. L. Jones
Primary Examiner
Art Unit 1616

March 4, 2005